REMARKS

The Office Action dated September 14, 2001 has been carefully reviewed and the foregoing amendments are made in response thereto. In view of these amendments and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Applicants respectfully submit that no new prohibited matter has been introduced by the amendments. Written description support for the amended claims can be found throughout the specification and in the original claims. In particular, support for the amended claims can be found on page 2, lines 6-15; page 3, lines 8-13; and page 8, lines 14-21.

Summary of the Office Action

1. Claim 12 has been withdrawn from consideration as being drawn to an invention of a non-elected group.

2. Claims 1-9 have been rejected under 35 U.S.C. 112 (second paragraph) as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention.

3. Claims 1-11 have been rejected under 35 U.S.C. 101 for lack of utility.

4. Claims 1-11 have been rejected under 35 U.S.C. 112 (first paragraph) on the grounds that the skilled artisan would not know how to use the claimed invention.

5. Claims 1-9 and 11 have also been rejected under 35 U.S.C. 112 (first paragraph) on the grounds that the specification does not enable the skilled artisan to use the invention commensurate in scope with these claims.

6. Claim 11 was rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 6,066,724.

Rejection Under 35 U.S.C. 112 (second paragraph)

Claims 1-9 have been rejected under 35 U.S.C. 112 (second paragraph), as purportedly being indefinite for failing to correlate back to the claim preamble. Applicants have amended claims 1 and 3 so that they now recite a step correlating back to the preamble, indicating that the presence of SEQ ID NO: 3 is associated with the presence of, or susceptibility to, cancer. Applicants respectfully submit that the amended claims are not indefinite as to whether the presence of SEQ ID NO: 3 is associated with the presence of, or susceptibility to, cancer. In view of the claim amendments and aforementioned remarks, Applicants request that the rejection under 35 U.S.C. 112 (second paragraph) be withdrawn.

Rejection Under 35 U.S.C. 101

Claims 1-11 have been rejected under 35 U.S.C. 101 purportedly because the specification does not support a specific asserted utility nor refer to a well-established utility. Applicants have amended the claims so that they are now related to screening for, or detection of cancer in an animal by testing for the presence of a protein having an N-terminal amino acid sequence as shown in SEQ ID NO: 3. Accordingly, Applicants submit that the invention as now claimed, has a significant and credible utility in the screening and detection of cancer.

Applicants respectfully submit that the utility of the method in detecting cancer in an animal is clearly set out in the specification as filed. Applicants further submit that the claimed utility is credible, specific and substantial. Confirmation of the claimed utility is discussed below and in the attached Rule 1.132 Declaration by Dr. Gary Cobon, an expert in the fields of proteomics and cancer research. The Declaration demonstrates that a protein comprising SEQ ID NO: 3 has been detected with much higher frequencies in patients with various types of carcinomas compared to normal controls (*i.e.*, subjects with no familial history of cancer) just as set forth in the specification. This protein has also been detected with increased frequency in subjects with a familial history of cancer compared to those without. Experimental data from laboratory experiments is included with the Declaration.

The Office Action purports that the identity of SEQ ID NO: 3 is not disclosed in the specification. The specification teaches, however, that SEQ ID NO: 3 is closely related to the uteroglobins (page 6, lines 11-16) and that uteroglobins include human mammaglobin (page 6, lines 17-22). The human mammaglobin referred to in the presence application is now designated as mammaglobin 1/mammaglobin A (see attached OMIM extract). The complete sequence of SEQ ID NO: 3 has subsequently been cloned and designated as mammaglobin 2/mammaglobin B (see attached OMIM extract), which is a uteroglobin.

On the basis of the similarity to mammaglobin A, the protein expression of which correlates with human breast cancer, and rat prostatic steroid-binding protein C3, the protein expression of which correlates with prostate cancer, Applicants have determined that the unexpected presence in tears of a protein comprising the sequence of SEQ ID NO: 3 should provide a readily accessible marker for cancerous conditions in animals.

Additional experimental data using control and cancer patients has confirmed SEQ ID NO: 3 as a cancer marker. Twenty-three cancer patients, two patients without tumors but a family history of cancer, and three controls with no family history of cancer and with no tumors were tested for the presence of mammaglobin B/lacryglobin (SEQ ID NO: 3) in their tears. The resulting data are presented in Exhibit A

of the attached Declaration. The data demonstrate that SEQ ID NO: 3 is expressed at higher levels in patients with a range of tumors, or with a genetic predisposition to cancer with no tumors (*e.g.*, those with a family history of cancer), than in control patients with no tumors and without familial history of cancer.

Applicants further submit that in view of the clear utility of the claimed method as set forth above, the skilled artisan would be able to practice the invention using the disclosure of the specification. In view of the claim amendments and aforementioned remarks, Applicants request that the rejections under 35 U.S.C. 101 & 112 (first paragraph) be withdrawn.

Rejection Under 35 U.S.C. 112 (first paragraph)

Claims 1-11 have also been rejected under 35 U.S.C. 112 (first paragraph) on the grounds that the specification is purportedly not enabled for a method of detecting non-ocular diseases comprising detecting a "part" of SEQ ID NO: 3 in tear samples. Applicants have amended the claims, without prejudice or disclaimer, and in order to expedite prosecution, to delete reference to "part" of SEQ ID NO: 3 (see claim 11, in particular), and that the presence of SEQ ID NO: 3 be used to screen for, and detect cancer. The amended claims now require that the entire sequence of SEQ ID NO: 3 be used in the claimed method. Applicants submit that in view of the claim amendments incorporating the feature that the entire protein sequence be used to screen for, and detect cancer, the claimed scope of the invention is appropriate, given the clear correlation between the presence of SEQ ID NO: 3 in tear samples from patients and the presence of various cancerous conditions in these same patients.

Applicants further submit that the claimed approach of detecting a protein having the sequence set forth in SEQ ID NO: 3 for the purpose of screening for cancer as set forth in the specification has clearly been validated by the attached Declaration. It would therefore not require more than routine experimentation by the skilled artisan to practice the claimed invention. In light of the aforementioned amendments and remarks, Applicants respectfully request that the rejection under 35 U.S.C. 112 (first paragraph) be withdrawn.

Rejection Under 35 U.S.C. 102

Claim 11 was rejected under 35 U.S.C. 102(b) as purportedly being anticipated by U.S. Patent 6,066,724. Applicants have amended this claim, without prejudice or disclaimer, and to expedite prosecution, to delete reference to a fragment of SEQ ID NO: 3. Applicants submit that the cited reference does not apply because the amended claim recites a polypeptide sequence comprising SEQ ID

NO: 3, while the reference discloses a sequence which is 98.6% similar to, but not identical to, the complete sequence of SEQ ID NO: 3. In view of the claim amendment and aforementioned remarks, Applicants respectfully request that the rejection under 35 U.S.C. 102(b) be withdrawn.

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request reconsideration and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, he is invited to telephone the undersigned at his convenience. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made" as required by the new rules.

If there are any other filing or claim fees due in connection with the filing of this amendment, please charge the fees t our Deposit Account No. 50-0310. If a fee is required for any extension of time under 37 C.F.R. 1.136 no accounted for above, such an extension is requested and the fee should be charged to our Deposit Account.

Dated: **March 14, 2002**
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Respectfully submitted
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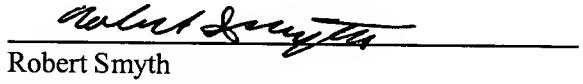

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claim 1 has been amended as follows:

1. (Twice Amended) A method of screening for, or detecting [~~non-ocular disease~~] cancer in an animal[~~, the method~~] comprising:

(a) obtaining a tear sample from the animal; and

(b) analyzing the tear sample for [~~an indicator or marker of the non-ocular disease, wherein the indicator or marker is~~] the presence of a protein having a N-terminal amino acid sequence comprising SEQ ID NO: 3; [~~selected from the group consisting of:~~
~~EDASSDSTGA DPAQ(E/Q)AGTSQ PNEDIAG (SEQ ID NO: 1);~~
~~WDPKE (SEQ ID NO: 2); and~~
~~DSGCKLLEDM VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN~~
~~QSHRTLKNFG LMMHTVYDSI WCNL (SEQ ID NO: 3)~~]
wherein the presence of the protein is indicative of predisposition to, or the presence of, cancer.

Claim 3 has been amended as follows:

3. (Twice Amended) A method of screening for, or detecting [non-ocular disease] cancer in an animal[~~, the method~~] comprising [the steps of]:

(a) obtaining a tear sample from the animal;

(b) separating biomolecules present in the tear sample; and

(c) detecting for the presence [~~or absence of one or more biomolecules such that the presence or absence of the one or more biomolecules being an indicator or marker of a disease state in the animal, wherein the one or more biomolecules are one or more proteins~~] of a protein having a N-terminal amino acid sequence comprising SEQ ID NO: 3; [~~selected from the group consisting of:~~
~~EDASSDSTGA DPAQ(E/Q)AGTSQ PNEDIAG (SEQ ID NO: 1);~~
~~WDPKE (SEQ ID NO: 2); and~~
~~DSGCKLLEDM VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN~~
~~QSHRTLKNFG LMMHTVYDSI WCNL (SEQ ID NO: 3)~~]
wherein the presence of the protein is indicative of the predisposition to, or the presence of, cancer.

Claim 6 has been amended as follows:

6. (Once Amended) The method according to claim [~~5~~] 3, wherein the cancer is breast or prostate cancer.

Claim 10 has been amended as follows:

10. (Twice Amended) An isolated protein which is detectable in tears [having] and has an N-terminal an amino acid [~~N-terminus~~] comprising SEQ ID NO: 3 [~~selected from the group consisting of: EDASSDSTGA DPAQ(E/Q)AGTSQ PNEDIAG (SEQ ID NO: 1); WDPKE (SEQ ID NO: 2); and of DSGCKLLEDM VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN QSHRTLKNFG LMMHTVYDSI WCNL (SEQ ID NO: 3)~~].

Claim 11 has been amended as follows:

11. (Twice Amended) An isolated protein which is detectable in tears [~~including~~] and which includes the amino acid sequence SEQ ID NO: 3 [~~: DSGCKLLEDM VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN QSHRTLKNFG LMMHTVYDSI WCNL (SEQ ID NO: 3) , or fragment thereof~~].